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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	4

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/731,830	Applicant(s) HAMURO ET AL
	Examiner Chih-Min Kam	Art Unit 1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is. a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/334,647* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-3 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S.Patent 6,197,749. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-3 in the instant application disclose a method of treating cachectic condition caused by cancers,....or autoimmune inflammatory diseases, comprising administering to a patient a composition comprising a substance which reduces the content of reductive glutathione in macrophages, wherein the substance suppresses cellular immune responses in patient. This is obvious in view of claims 1-3 in the patent which disclose a method of treating cachectic condition caused by cancers,....or autoimmune inflammatory diseases, comprising administering to a patient a composition comprising a cystine derivative which reduces the content of reductive glutathione in macrophages and suppresses cellular immune responses in patient. Both sets of claims treat cachectic condition caused by the same disease with a composition comprising a substance (the present application) and a cystine derivative (the

patent) which can reduce the reductive glutathione and suppresses cellular immune responses in patient. Thus, claims 1-3 in present application and claims 1-3 in the patent are obvious variations of treating cachectic condition with a substance including a cystine derivative which can reduce the content of reductive glutathione in macrophages and suppresses cellular immune responses in patient.

2. Claim 11 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 10 of U.S.Patent 6,197,749. The conflicting claims are identical because claim 11 in the instant application discloses a method of suppressing immune responses, wherein the substance is a compound in which a cytotoxic DNA alkylating agent is conjugated with glutathione, or one which shows a cytotoxicity after being incorporated into macrophages as precursor. This is obvious in view of claim 10 in the patent which disclose a method of suppressing immune responses, wherein the substance is a compound in which a cytotoxic DNA alkylating agent is conjugated with glutathione, or one which shows a cytotoxicity after being incorporated into macrophages as precursor. Both sets of the claim suppress immune responses with the same substance in the present application and the patent. Thus, claim 11 in present application and claim 10 in the patent are obvious the same method of suppressing immune responses with the same substance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph.

Claims 1-2 are rejected because the specification, while being enabling for a method of treating cachectic condition caused by cancers.....or autoimmune inflammatory diseases, comprising administering to a patient an effective amount of composition comprising a cystine derivative which reduces the content of reductive glutathione in macrophages does not reasonably provide enablement for a method of treating cachectic condition comprising administering to a patient an effective amount of composition comprising a substance which reduces the content of reductive glutathione in macrophages. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-2 are drawn to encompass a method of treating cachectic condition caused by cancers.....or autoimmune inflammatory diseases, comprising administering to a patient an effective amount of composition comprising a substance which reduces the content of reductive glutathione in macrophages. The specification, however, only discloses cursory conclusions (see page 4, line 19-22) which states that a method of treating cachectic condition caused by cancers.....or autoimmune inflammatory diseases, comprising administering to a patient an effective amount of composition comprising a substance which reduces the content of reductive glutathione in macrophages. There is no disclosure or description of a substance other than cystine derivative to reduce the content of reductive glutathione in macrophages. Despite knowledge in the art for the biological function of glutathione, the claims encompass enormous numbers of compounds that can reduce the content of glutathione in cells which would not be expected by the skilled artisan to accomplish the goal set forth. For example, glutathione can react enzymatically (glutathione S-transferases) and nonenzymatically to form glutathione S-

conjugates with endogenous compounds (e.g., leukotriene A, estrogens, prostaglandins) and exogenous compounds (e.g., bromobenzene, melphalan), and depletion of cellular glutathione can be reached by treating a patient with inhibitors of γ-glutamylcystiene synthetase (See US patent 5,476,966, col. 1, line 54-63). Thus, the claims are directed to specifically encompass enormous numbers of embodiments for which it is not expected to be known whether the embodiments are inoperative or operative in the same manner as cystine derivative. Since it is not routine in the art to engage in *de novo* experimentation where the expectation of success is unpredictable, the skilled artisan would require additional guidance in order to use such compound in a manner reasonably commensurate with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite, because of the use of the term "cystine derivative". The term "cystine derivative" renders the claim indefinite, it is not clear what kind of cystine compound is intended as compared to cystine.

5. Claim 11 is indefinite because of the use of the term "said substance is a compound in which a cytotoxic DNA alkylating agent is conjugated with glutathione". The term "said

substance is a compound in which a cytotoxic DNA alkylating agent is conjugated with glutathione" renders the claim indefinite, it is unclear in the claim whether the substance is a cytotoxic DNA alkylating agent or a conjugate of a cytotoxic DNA alkylating agent with glutathione. For example, the substance in claim 11 appears to be a cytotoxic DNA alkylating agent which reduces the content of reductive glutathione in macrophages as cited in claim 1, since claim 11 is dependent on claim 1 and should meet the limitation of claim 1. However, claim 11 also recites a substance is a compound of a cytotoxic DNA alkylating agent conjugated with glutathione.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Anderson *et al.* (U.S. Patent 5,476,966)

Anderson *et al.* teach a method of decreasing glutathione levels in cells and tissues by administering S-substituted homocysteine sulfoximines to a patient to reduce glutathione levels which is useful for chemo- and radio-treatment of tumors and parasites (col. 1, lines 18-21, 54+; col. 7, lines 1-50). The administration of such compound which reduces glutathione levels in cells and produce a desired effect on the patient with cancer chemothrapy and/or radiation therapy would be expected to treat cachectic condition caused by cancers (claim 1).

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8:00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D.
Patent Examiner

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May 11, 2001

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER